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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Roy Christiaan Montijn

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27387

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NORRIS, MCLAUGHLIN & MARCUS, P.A.

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EXAMINER

WOOD, AMANDA P

ART UNIT

PAPER NUMBER

1657

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

03/12/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,496	MONTIJN ET AL.	
	Examiner	Art Unit	
	Amanda P. Wood	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11 December 2006 has been entered.

Claims 1-13 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, claim 1 recites the phrase "determining an environmental condition of which the effect on one or more microorganisms is unknown comprising measuring a natural biochemical composition...where said composition specifically changes...the induction route that leads to the change in the biochemical composition is unknown." Claims 2 and 3 recite nearly identical claim language to that of claim 1, particularly the limitations that the effect of the environmental condition on the

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microorganism is unknown and that the induction route that leads to the change in the biochemical composition is unknown. In addition, claim 13 recites the phrase, "determining an environmental condition without identification of the effect of such environmental condition on one or more microorganisms comprising measuring a natural biochemical composition" in lines 1-4. It is unclear how one of skill in the art would be expected to know what natural biochemical composition to measure in said microorganism if the effect of the environmental condition on said microorganism is not identified. In addition, it is unclear how one of ordinary skill in the art would be expected to determine an environmental condition in which a microorganism has been placed if the effect of the environmental condition on said microorganism is unknown (i.e., what to measure for is unknown) and if it is also unknown what leads to the change (i.e., what is the induction route or what condition causes the change). Furthermore, Applicant has given no guidance in the instant specification as to how one of ordinary skill in the art would determine what natural biochemical composition to measure, and whether the biochemical composition is something found in a microorganism, or in the environment. With respect to the instant specification, Applicant merely states (on page 3, lines 14-17) that "in principle, a large number of environmental conditions can be deduced therefrom, in principle without it being necessary that the induction routes that lead to the change are known." Applicant has provided no clear examples in the instant specification teaching one of skill in the art how to make and use the invention, as claimed. In addition, Applicant has given no guidance as to how one of skill in the art would determine an environmental condition, or determine a change in an environmental condition without knowledge of how the condition affects the microorganisms which are being exposed to it, and furthermore, without such knowledge, it would require undue experimentation to determine what biochemical compositions, and therefore, biomolecules, would need to be measured, to make the necessary measurements for practice of the instantly claimed invention.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, first paragraph for the reasons set forth above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase measuring a natural biochemical composition by detecting qualitatively or quantitatively a plurality of different biomolecules..." in lines 3-4. Claims 2 and 3 recite nearly identical claim language to that of claim 1, particularly the limitations involving measuring a biochemical composition by detecting biomolecules. It is unclear whether the biomolecules being detected are components of the natural biochemical composition, or whether they are something made by the microorganism in response to the presence of the biochemical composition and/or due to exposure to the environmental condition, or are something else entirely. Furthermore, Claims 1, 2, and 3 recite the phrase "the induction route that elads to the change in the biochemical composition is unknown." It is unclear what exactly Applicant means by the term "induction route" and how one of skill in the art would be expected to know what biochemical composition to measure in a particular microorganism, what change in said composition to measure, and under what conditions said measurement should be made, in order to practice the claimed invention. In addition, claim 13 recites the phrase, "determining an environmental condition without identification of the effect of such environmental condition on one or more microorganisms comprising measuring a natural biochemical composition" in lines 1-4. It is unclear how one of skill in the art would be expected

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to know what natural biochemical composition to measure in said microorganism if the effect of the environmental condition on said microorganism is not identified.

Claim 1 recites the limitation "the effect" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 2 recites the limitation "the effect" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 3 recites the limitation "the effect" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 13 recites the limitation "the effect" in line 1. There is insufficient antecedent basis for this limitation in the claim.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Based upon the indefinite nature of the instant claims, a further search was unable to be performed on the claims. Therefore, the following references appear to be the closest prior art.

Claim Rejections - 35 USC § 103

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duncan et al (Letters in Applied Microbiology 2000) in view of Larossa et al (US 6,607,885), and further in view of Bott et al (Water Science and Technology 2001).

A method for determining an environmental condition of which the effect on one or more microorganisms is unknown by measuring a biochemical composition of one or more microorganisms exposed to said environmental condition is claimed.

Duncan et al teach a method of determining whether toxic compounds have perturbed a wastewater treatment process (i.e., an environmental condition) by measuring the amount of a

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stress protein (i.e., a biochemical composition) expressed by the diverse population of microorganisms in the wastewater treatment process. Furthermore, Duncan et al teach that changes in the environmental condition of the treatment process can be monitored by measuring the changes in the amount of stress protein expressed by these microorganisms (i.e., qualitative or quantitative measuring), and that protein induction patterns, or protein fingerprints (i.e., plurality of different proteins or biomolecules), in these activated sludge cultures can be determined and used in monitoring the treatment process (see, for example, Abstract and Introduction, pgs 28-29). Duncan et al teach that a diverse population of microorganisms exist in these activated sludge cultures, but in particular, *E. coli*, *Rhodobacter sphaeroides*, *Nitrosomonas europaea*, *Sphingomonas capsulata* and *Pseudomonas putida* were used by Duncan et al. In addition, Duncan et al measured the amount of the general shock protein GroEL that was induced in the cells of these bacteria in response to the contamination of the wastewater treatment process (i.e., a bioconversion process in an aqueous environment) under different environmental conditions. Duncan et al further teach that relative levels of stress proteins in conjunction with their induction patterns will lead to the development of a useful monitoring technology based upon microbial stress response.

Duncan et al do not specifically teach a method wherein the biochemical composition is the transcriptome (i.e., measurement of mRNA levels present in a cell), nor a method wherein the biochemical composition is determined using microarrays.

Larossa et al beneficially teach a method wherein the effect of environmental changes is determined by measuring gene expression levels (i.e., the transcriptome) in bacteria. Larossa et al specifically teach that *E. coli* experiments to define stress-related responses in the past have used mRNA measurements to determine an individual gene's expression profile (see, for example col. 1, lines 30-60 and col. 2, lines 20-65).

In addition, Larossa et al beneficially teach a method wherein a bacterial species is subjected to a gene expression altering condition (i.e., an environmental condition) and a microarray of the bacterial RNA is generated so as to identify the gene expression level and changes in the bacteria. Furthermore, Larossa et al beneficially teach that it is possible to monitor the effect of environmental changes on gene expression by comparing expression levels of genes from bacteria that have not been exposed to stress to those of bacteria that have been exposed to stress.

Bott et al beneficially teach that stress proteins are readily induced in bacteria in response to a broad range of environmental stress conditions, including heat, starvation, and anaerobiosis. In addition, Bott et al beneficially teach that it is possible to identify a range of indicator proteins that are rapidly induced in response to stress, and that these proteins may provide valuable information about the health of the environmental system being studied (see, for example, Abstract, and pg. 124).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods disclosed by Duncan et al based upon the beneficial teachings provided by Larossa et al, with respect to the art-recognized method of using microorganisms to monitor an environmental condition or changes in a condition, and by Bott et al, with respect to the teaching that a plurality of bacterial stress proteins exist and could be used as indicators of an environmental condition, as discussed above. Furthermore, the cited references particularly point out that the level of a protein such as a stress protein or heat-shock protein (i.e., a biochemical composition) can be measured in bacteria that have been exposed to an environmental condition, such as contamination by toxic compounds, and that it would be beneficial to develop a monitoring technology using relative levels of stress proteins in conjunction with their induction patterns. In addition, the cited references particularly point out

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that microarrays can be used to determine the amount of RNA or protein a microorganism, such as bacteria, expresses upon exposure to a stressor, such as a change in environmental condition, and therefore, it would have been obvious and beneficial for the skilled artisan to use the methods taught by Duncan et al so as to determine an environmental condition by measuring a biochemical composition of one or more microorganisms. The result-effective adjustment of particular conventional working conditions (e.g., using a particular microorganism, measuring a particular number of biochemical compositions, and/or using a particular method to determine the biochemical composition) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Applicants' arguments concerning the above USC 103 rejection have been carefully considered but are not deemed to be persuasive of error in the rejection. Applicant argues that Bott et al merely contend that it may be possible to identify a range of indicator proteins that are induced in response to different mechanisms of stress in microorganisms. However, the Examiner would like to point out that Applicant may have taken out of context Bott et al's teachings, wherein the phrases quoted by Applicant were intended to showcase the concepts Bott et al intended to test in the instant article (see, for example, Bott et al, second full paragraph pg 124).

Conclusion

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No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda P. Wood whose telephone number is (571) 272-8141. The examiner can normally be reached on M-F 8:30AM -5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner
Art Unit 1657

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CHRISTOPHER R. TATE
PRIMARY EXAMINER